March 16, 1998

Amendments to the Specification

Please replace the paragraph beginning at page 6, lines 1-3, with the following rewritten paragraph:

--"GIRK1/KGA" and "KGB" are renamed Kir3.1. The Genbank accession numbers for these sequences, from different species, are L25264 (SEQ ID NO:7); U01071 (SEQ ID NO:8); U01141 (SEQ ID NO:9); and D45022 (SEQ ID NO:10).--

Please replace the paragraph beginning at page 6, lines 4-9, with the following rewritten paragraph:

-- "GIRK2" is renamed a Kir3.2. The Genbank accession numbers for these sequences, from different species, are U011860 and U24660 (SEQ ID NO:11). "GIRK3" is renamed a Kir3.3. The Genbank accession numbers for this sequence isU11860 (SEQ ID NO:12). "GIRK4", "rcKATP/CIR", "hcKATP" is renamed a Kir3.4. The Genbank accession numbers for these sequences, from different species, are X83584 (SEQ ID NO:13); L35771(SEQ ID NO:14); X83582(SEQ ID NO:15); and L47208 (SEQ ID NO:16).--

Please replace the paragraph beginning at page 4, lines 9-15 with the following rewritten paragraph:

-- Figures 1A-C show[s] inward currents evoked by high K⁺, 5HT and ACh in RNA-injected oocytes.

(A) I_{hk} and I_{5HT} in an oocyte injected with atrial RNA + 5HT1A-R RNA. Holding potential in this and all following figures was -80mV. (B) Inward currents evoked by ACh (AcCHo) and 5HT in a single oocyte in hK solution. (C) The dependence of I_{5HT} amplitude on 5HT concentration in oocytes of one frog. In each oocyte, the response to one 5HT concentration was tested. Data represent mean±SEM in 4-6 cells at each concentration.--

Please replace the paragraph beginning at page 4, lines 16-26 with the following rewritten paragraph:

-- Figures 2[.]A-D depict that I_{hk} and I_{5HT} are inwardly rectifying K⁺ currents. (A) Currents evoked by voltage steps from the holding potential of -80 mV to voltages between -140 and 40 mV in 20 mV steps

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in ND96(a), hK (b), hK in the presence of 5HT (c). Net I_{5HT} (d) was obtained by digital subtraction of (b) from (c). (B) Current-voltage relations of the total membrane current in a representative oocyte in NG 96 (2 mM [K_{out}]; \square), in 25 mM [K⁺_{out}] \spadesuit); in 75 mM [K_{out}] \bigcirc , and in hK (96 mM [K_{out}]; \blacktriangle). (C) Current-voltage relation of the net I_{5HT} in the same oocyte as in (B) in 25 mM [K_{out}] \spadesuit); 75 mM [K_{out}] \bigcirc , and 96 mM [K_{out}] \spadesuit . (D) The dependence of the reversal potentials of total membrane current \spadesuit and of I_{5HT} \spadesuit on [K_{out}]. The straight lines represent least square fits to data (mean±SEM, n=3 for each point).--

Please replace the paragraph beginning at page 4, lines 27-28 with the following rewritten paragraph:

-- Figures 3[.]A-D depict the Ba²⁺ block of I_{hk} and I_{5HT} . (A-C)[,] show records taken from the same oocyte at 10 min intervals. Between the records, the cell was bathed in ND96. 5HT concentration was 4 nM. Note that in (B) 300 *M Ba²⁺ reduces I_{hK} and almost completely blocks I_{5HT} . Ba²⁺ and 5HT were washed out simultaneously, and this resulted in an inward current "tail". (D) dose dependence of BA²⁺ inhibition of I_{hK} in native oocytes \bigcirc , I_{hk} in RNA-injected oocytes \bigcirc , I_{5HT} in RNA-injected oocytes. Data are mean±SEM, n=3 to 7 for each point.--

Please replace the paragraph beginning at page 5, lines 7-13 with the following rewritten paragraph:

-- Figures 4[.]A-B depict that I_{5HT} is mediated by activation of a G-protein. (A) The effect of PTX treatment (500 ng/ml, 20-26 h) on I_{hK} and I_{5HT} . The cells were injected with 120 ng/oocyte total atrial RNA, 11 ng/oocyte 5HT1A-R RNA, and, where indicated, with 11 ng/oocyte G_{i2} * RNA. (B) GDP-*-S injection inhibits I_{5HT} but not I_{hK} in an oocyte injected with atrial + 5HT1A-R RNAs. 5HT concentration was 0.4 *M. A small outward current deflection (denoted by \bigstar) upon washout of 5HT was caused by an inadvertent perfusion of ND96 for a few seconds.--